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DRUG DISCOVERY

APMP - a web database for Active Principles in Indian Medicinal Plants

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ABSTRACT

Plants represent the eternal kindness of nature by all means which is really expressed in varied human culture from time immemorial. Many of the modern medicines are produced indirectly from medicinal plants, for example aspirin. Medicinal plants can provide biologically active molecules and lead structures for the development of modified derivatives with enhanced activity and /or reduced toxicity. Drug development based on natural product is an important and fast growing area due to the limitations of developing new synthetic molecules based on the principle of active components or pure chemicals. The scientific study of traditional medicines, derivation of drugs through bioprospecting and systematic conservation of the concerned medicinal plants are thus of great importance. In order to improve the information about active principles we created a APMP (Active Principles in Indian Medicinal Plants) database with textual and graphical based web applications. The database was developed as relational database which incorporates the structural information and annotated data of active constituents, toxicological, biochemical, pharmacological activity and technical data. APMP provides an external links to online databases and internal links every active principle which contains molecular descriptors, SMILES notation as well as for each plant as well every plant details. The database was fabricated using a DBMS (MySql); an application server (Apache), a server side scripting language (PHP) .APMP is freely accessible via the World Wide Web at URL http:/scbt.sastra.edu/apmp

Keywords: Active principles, descriptor, antimicrobial, drug design, SMILES.

Abbreviations: DBMS- Database Management System, SQL- Structured Query Language, JME- JAVA Molecular Editor.

1. INTRODUCTION

Plants have traditionally been used as a source of medicine in India by indigenous people of different ethnic groups inhabiting various terrains for the control of various ailments afflicting human and their domestic animals (Manju Panghal et al., 2010). According to the World Health Organization (WHO, 1977) “a medicinal plant” is any plant, which in one or more of its organ contains substances that can be used for the therapeutic purposes or which, are precursors for the synthesis of useful drugs. Medicinal plants are plants containing inherent active ingredients used to cure disease or relieve pain (Okigbo et al., 2008). Around 100 plant species have contributed significantly to modern drugs. The medicinal properties of plants could be based on the antioxidant, antimicrobial, antipyretic effects of the phytochemicals in them (Cowman, 1999; Adesokan et al., 2008). For example phytochemicals (such as alkaloids, tannins, flavonoids and terpenes) present in active extracts, tannins and flavonoids are thought to be responsible for antidiarrhoeal activity by increasing colonic water and electrolyte reabsorption (Palombo et al., 2006). Most plant parts (extract) identified eg.(bark root, seeds, fruit, leaf) serve as major source of active ingredient and products of secondary metabolites e.g alkaloid, terpenoids etc used in curing diseases, production of drugs as well as in maintaining good health by both the traditional and orthodox medical practitioners (Nwachukwu C. U et al.,2010). The traditional uses of plants containing oleanolic acid or ursolic acid in folk medicines are multiple, in terms of antiinflammatory, hepatoprotection, analgesia, cardiotonic, sedative and tonic effects, etc. (Jie Liu, 1995). These principles may vary throughout a species and on plants of the same species according to various factors. However, many medicinal plants also possess toxicological properties which are largely dependent on the concentration of the active principle. In case of Purple Foxglove, the biochemical active compound, Digitalis purpurea, increases the muscle contraction ability of the heart, but on the other hand it reduces the pulse rate significantly which is an unwelcome side effect Medicinal plants continue to play a significant role as a resource for the discovery of novel drugs. Approximately 75% of these substances were discovered as a direct result of chemical studies focused on the isolation of active substances from plants used in traditional medicine (Cragg and Newman, 2001a; Cragg and Newman, 2001b, Spainhour, 2005). Drug development based on natural product is an important and fast-growing area due to the limitations of developing new synthetic molecules based on the principle of active components. This provides new and important leads against various pharmacological targets including cancer, HIV/AIDS, Alzheimer's, malaria, and pain. Drug design involves a two-step pre-clinical process. The first step is to identify and model the biological target within the body (the protein). The second step involves identifying a lead compound (molecule) that exhibits drug-like properties with respect to this protein. The identification of a lead involves species with known biological activity whose active compound have not been isolated (e.g., traditionally used herbal remedies) or involves taxa collected randomly which are then subjected to screening. Databases are available for finding the target for many diseases, but there is no comprehensive database for finding the lead molecules for the target. Therefore, the APMP serves as a database for finding the potential lead molecules (10). Since there is a

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Table1: APMP showing Family details and their respective Medicinal Plant and active principles. (Here a partial list is provided)

S.No.	Family Name	Plant Name	Active Compound
1	Malvaceae	Abelmoschus esculentus (Linn.)Moench.	quercetin, hyperin
		Abutilon indicum Linn. Sweet.	mucilage,tannins, asparagines
		Althaea officinalis Linn.	mucilage,pectin, flavonoids
2	Pinaceae	Abies pindrow Royle	Terpenoids,flavonoids, glycosides
		Abies webbiana Lindl.	beta-sitosterol
		Picea smithiana Boiss	alpha-pinene
3	Sterculiaceae	Abroma augusta Jacq	abromine (betaine), friedelin
		Kleinhovia hospita Linn.	quercetin and rutin.
		Waltheria indica Linn.	pelargonidin and cyanidin glycoside
4	Euphorbiaceae	Acalypha indica Linn	Kaempferol
		Kirganelia reticulata (Poir) Baill	beta-sitosterol
		Mallotus philippensis Muell.-Arg	Methylphloroacetophenone
5	Sapotaceae	Achras zapota Linn	Quercitol
		Madhuca butyracea Macr	beta-amyrin acetate, friedelin
		Madhuca indica J. F. Gmel	beta-sitosterol
6	Adiantaceae	Actiniopteris dichotoma Kuhn	Rutin
		Adiantum capillus-veneris Linn	rutin, isoquercetin
		Adiantum lunulatum Burm	chlorophyll-degradation products
7	Papilionaceae	Abrus precatorius Linn.	abrasine and precasine
		Alhagi pseudalhagi (Bieb.) Desv.	Alhagimanna
		Cajanus cajan (Linn.)Millsp.	riboflavin and pyridoxine.
8	Amaranthaceae	Achyranthes aspera Linn.	Ecdysterone
		Achyranthes bidentata Blume	oleanolic acid
		Aerva javanica (Burm. f.) Juss. ex Schul	beta-amyrin and beta-sitosterol
9	Adiantaceae	Actiniopteris dichotoma Kuhn.	Rutin
		Adiantum aethiopicum Linn.	rutin, isoquercetin
10	Leguminosae	Adenanthera pavonina Linn.	Octacosanol
11	Cycadaceae	Zamia angustifolia Jacq.	bilobetin,gink-getin and sciadopitysin
12	Bignoniaceae	Jacaranda acutifolia auct. non-Humb. B	lupenone and beta-sitosterol
		Kigelia pinnata (Jacq.) DC.	Napthoquinones
14	Mimosaceae	Acacia arabica Willd. var. indica Benth	galactose; l-arabinose,l-rhamnose
		Acacia catechu (Linn. f.)Willd.	Catechin
		Acacia chundra Willd.	Catechin

continuous rapid increase in the number of commercially available drugs derived from plant sources, there is a distinct need for an easy accessible data collection that caters detailed scientific information on such plants and drugs either extracted from or contained in these natural sources. Thus developing a Medicinal plant database with active principles which provides updated information and multimedia data on botanical, toxicological, biochemical as well as pharmacological properties of medicinal plants can steer the process of Drug discovery and Drug design.

2. APMP CONSTRUCTION AND CONTENT

The database APMP aims to integrate the active constituents of the medicinal plants and thus facilitates the canvassing of the therapeutic value by finding the lead molecules which are essential in the process of Drug designing. The curated entries in the database where collected from many articles published in peer reviewed journals and online web resources. Figure1 depicts the overall functionality of APMP database.Three-tier architecture model is employed in the database, which is the fundamental framework for the logical design model, segments an application's components into three tiers of services. First a relational database management system MySQL is used to store and access the database “on the fly”. Annotations were

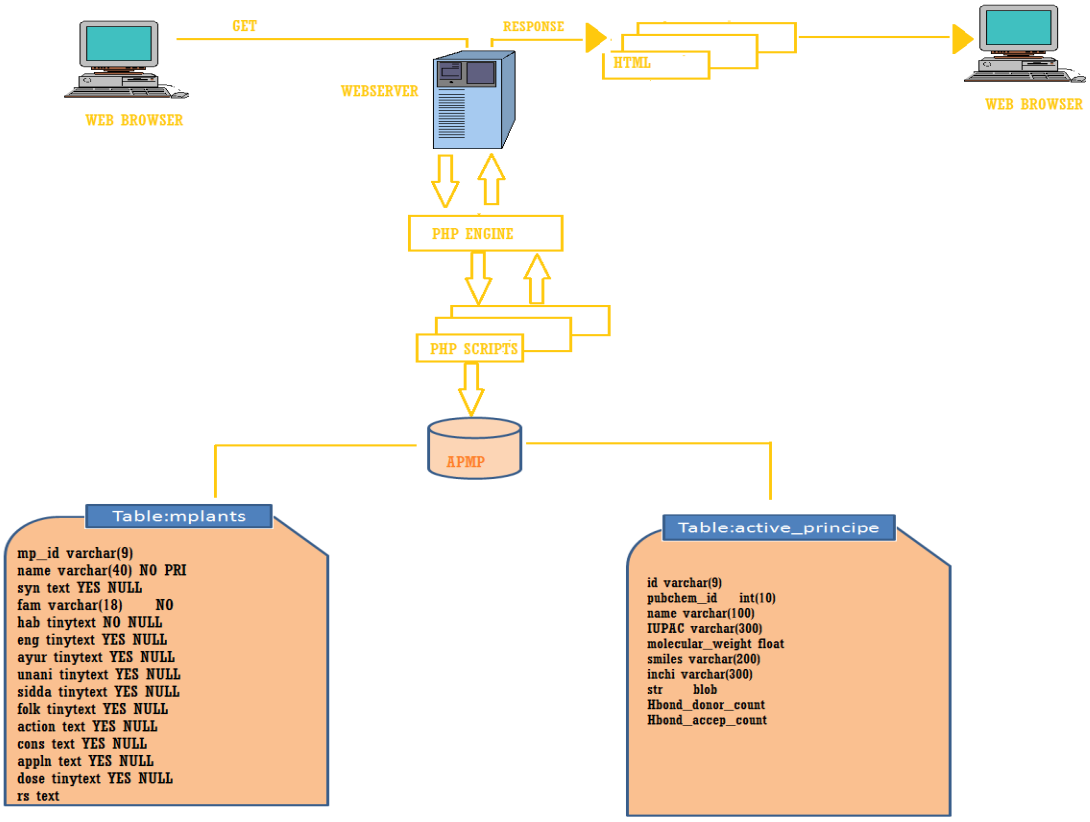

Figure 1
System Architecture of APMP database management system

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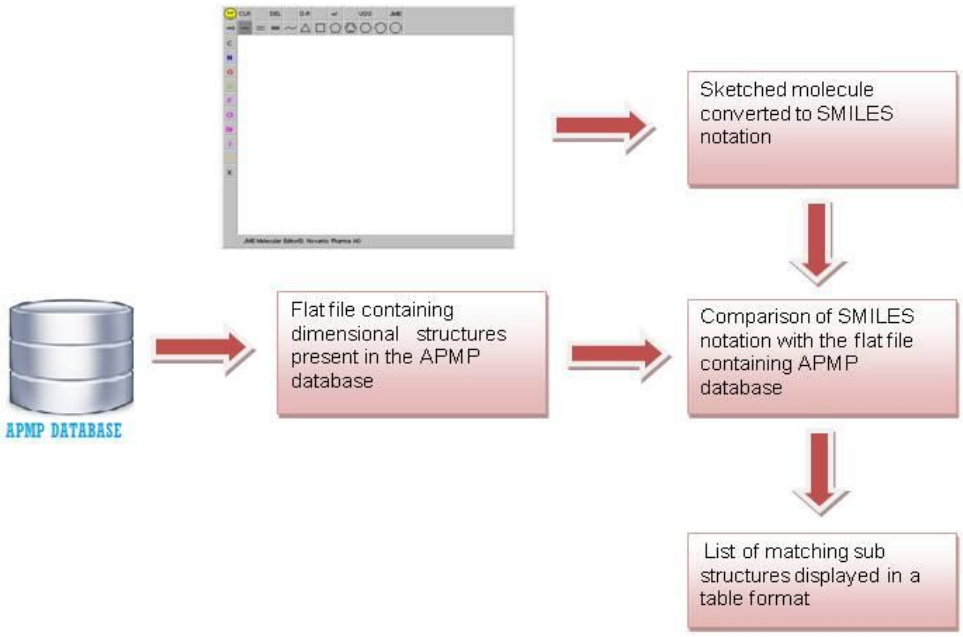

Figure 2

Substructure search implementation in APMP database

is a server-side database it requires a network connection. The structure of the APMP database system shows the organization of data in the form of tables. The primary table contains the information about Medicinal plants details with the fields MP_id, botanical name, Syn, Family, Habitat, Engligh, Ayurvedic, Unani, Sidda, Folk, Action, Constituents, Application, Dose, Related Species. MP_id is used as database constraint to identify a each entry in the database. The secondary table contains the fields (id, Pubchem_id, name, IUPAC, molecular_weight, smiles, inchi, str, Hbond_donor_count, Hbond_accep_count, rotatable_bond) for the active principle present in plants. The current version of the database has more than 400 Medicinal plants which has extensive coverage of active principles are shown in Table1

2.1. APMP Search Interface

The Homepage (Figure 3A) of APMP shows the links to many web graphical interfaces for searching and browsing information from the database. APMP interface should provide mechanisms for both textual and graphical based search. A text-based search engine (Figure3B) using PHP is used to query the database using

Figure 3

Home Page of APMP database shows various links to many web interface(A).Text based search Page to query the database (B).Hits matching the query term displayed in a table format with hyperlinks(C).Detailed view of each entry in the APMP database(D).Properties of active principle present in the Medicinal Plants(E).JME editor to draw and sketch molecules (F).Substructure results for the sketched molecule in JME which has internal link to APMP (G).APMP Browse interface to browse the database annotations using[Botanical name,Active Principle name](H).Alphabetical List of Active principle names(I).Table showing medicinal plant name after a selection is made in the active principle name

loaded using MySQL query browser, the easiest visual tool for creating, executing, and optimizing SQL queries. Second, Internet Information Services(IIS) server on a Solaris 10 operating system (QUAD CORE Xeon processor) as the Application server and finally PHP ,a widely used scripting language in many websites is used to query the database and generate the dynamic searches .Since APMP

anyone of the attributes such as Active Principle Name (ex: hyperin), Activity Search (ex: antitumor) and Family search (ex: Malvaceae). This search also serves the purpose of finding exact phrase as well as entries that contain the given words and displays the matched entries by combining almost all of the available fields of the database .The result page retrieves the Number of matched entries along with the information which has internal link provided to each matched entry the get the full annotation. Substructure Search

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(Figure 3F) allows user to draw the chemical structure in Java Molecular Editr (JME).The sketched molecule is converted to SMILES notations and compared with the with the APMP database. Figure 2 shows the implementation of substructure search in APMP database.The hits matching the query are displayed where a hyperlink is provided to each active principle names showing its available in Medicinal Plants.An online tool to browse the database annotations based on the alphabetical order of Active principle names, based on the Botanical names of Plants .A pagination based browse options enables user to quickly navigate the database entries.

3. CONCLUSION

The medicinal properties of plant species have made an outstanding contribution in the origin and evolution of many traditional herbal therapies. The identification of active principles and their transformation into medicines is one of the goals of medicinal chemistry. Drug discovery from medicinal plants involves a multifaceted approach which combines botanical, phytochemical, biological, and molecular techniques. There is a need for computational representation of 2D structure, need to be able to organize thousands of active compounds into meaningful groups. The database will be useful for the pharmaceutical industry involved in the early discovery of lead drug candidates for a given target disease. A graphical web interface was developed to explore the database and server in many ways. The database will be updated on a periodically to provide more information about the active principles.

DISCLOSURE STATEMENT

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